

COMMITTEE ON ORTHOPOXVIRUS INFECTIONS

Report of the fourth meeting

After the eradication of smallpox had been confirmed by the World Health Assembly in 1980, WHO commenced a 5-year programme to implement the post-eradication policies adopted by the Assembly in resolution WHA33.4. This programme had been recommended by the Global Commission for the Certification of Smallpox Eradication and was designed both to allay any fears that smallpox might recur and to provide for full documentation of the effort. The progress of the post-eradication programme has been reviewed year by year. In 1981 there was a meeting on the implementation of post-smallpox eradication policy which was followed by 3 meetings of the Committee on Orthopoxvirus Infections: 3-5 March 1982,¹ 15-17 March 1983² and 28-30 March 1984.³ The fourth meeting of the Committee on Orthopoxvirus Infections held in Geneva 24-26 March 1986 was charged with reviewing the implementation of the 19 recommendations on post-eradication policy made to the World Health Assembly by the Global Commission and recommending policies to be followed by WHO from 1986 onwards.

The meeting reviewed the implementation of the post-eradication policy, paying particular attention to the present and future status of variola virus stocks, the WHO emergency reserve of smallpox vaccine, the surveillance of human monkeypox and progress in documentation of the programme.

1. Vaccination policy (Global Commission recommendations 1 and 2)

WHO has been informed that all of its Member States have discontinued routine vaccination. No country in the world now requires a certificate of smallpox vaccination from international travellers.

The latest reports received by WHO concerning vaccine production and distribution by laboratories show that in 1984, 7 countries produced batches of smallpox vaccine totalling 3.8 million doses. Some of this production was for vaccination of military personnel. Ten countries, however, have already informed WHO that they no longer vaccinate their military personnel against smallpox.

Substantial progress has been made in the development of recombinant strains of vaccinia, capable of inducing immunity to several infectious pathogens. The Committee expects that human trials with such vaccines may soon be instituted and that various strains of recombinant vaccinia virus may in future be produced

¹ See No 14, 1982, pp. 105-109

² See No 20, 1983, pp. 149-154

³ See No 24, 1984, pp. 181-185

COMITÉ DES INFECTIONS À ORTHOPOXVIRUS

Rapport de la quatrième réunion

Une fois l'éradication de la variole confirmée en 1980 par l'Assemblée mondiale de la Santé, l'OMS a mis en place un programme quinquennal pour exécuter les politiques post-éradication adoptées par l'Assemblée dans sa résolution WHA33.4. Ce programme, recommandé par la Commission mondiale pour la Certification de l'Eradication de la Variole, était destiné à dissiper toute crainte de réapparition de la variole et à produire une documentation complète sur les efforts déployés. Les progrès accomplis par le programme post-éradication ont été passés en revue année après année. En 1981, s'est tenue une réunion sur la mise en œuvre de la politique post-éradication de la variole, suivie de 3 réunions du Comité des Infections à Orthopoxvirus: du 3 au 5 mars 1982,¹ du 15 au 17 mars 1983,² et du 28 au 30 mars 1984.³ La quatrième réunion du Comité des In

and used in immunization programmes. A clear distinction has to be made between routine smallpox vaccination which is now universally discontinued and the use of modified strains of vaccinia virus as vectors for use in immunization programmes against other diseases. Such a new use for vaccinia virus had not been foreseen when the Global Commission formulated its recommendations to WHO. A committee to coordinate the development of recombinant vaccinia antigens has been set up by WHO under the auspices of the Microbiology and Immunology Support Services of the Division of Communicable Diseases.

The Committee considered that Global Commission recommendations 1 and 2 had been fully implemented and commended WHO for its role in this achievement.

2. Reserve stocks of vaccine (Global Commission recommendations 3, 4, 5 and 6)

WHO maintains reserve stocks of smallpox vaccine sufficient to protect 200 million people, using the bifurcated needle. The 7.4 million doses packaged for use with jet injectors have been destroyed, as recommended at the third meeting of this Committee in 1984, and after consultation with the countries which had donated this vaccine. The remaining stocks are stored in 2 locations (Geneva and Lausanne) and periodic testing of samples for potency has assured the continuing good quality of this vaccine.

The Committee was informed that more than 102 million doses of smallpox vaccine are held in 22 countries and that storage conditions for at least 80% of these stocks are satisfactory. Taking into consideration the facts that nearly 10 years have elapsed since the last case of endemic smallpox and that human monkeypox has not proved to be a significant human disease problem (see section 5), the Committee felt that an unforeseen emergency was now so unlikely that it was no longer necessary for WHO to maintain a global vaccine reserve.

The Committee was informed that seed lots of smallpox vaccine virus continued to be held in 4 WHO collaborating centres.

3. Investigation of suspect cases (Global Commission recommendations 7 and 8)

The Committee was informed that the number of rumours of suspect cases reported to WHO had gradually declined from 31 in 1980 to 10 in 1985. Suspect cases had been adequately investigated by the relevant national authority with assistance from WHO collaborating centres and WHO epidemiologists. None had proved to be smallpox. The Committee believed that there will continue to be rumours and although investigation of most can safely be left to the medical authorities of the Member States, WHO participation and expertise may be needed in some instances to maintain confidence in the fact of eradication.

4. Retention of variola virus stocks (Global Commission recommendations 9 and 10)

The 2 laboratories which continue to hold stocks of variola virus, namely the Centers for Disease Control (CDC), Atlanta, United States of America, and the Research Institute for Viral Preparations, Moscow, USSR, were visited most recently by WHO inspection teams in November 1985 and January 1986 respectively. The inspection reports were satisfactory for both laboratories. Culture of variola virus has ceased at both laboratories and neither has plans to resume experiments involving culture of this virus.

The Committee reviewed the need for retaining the remaining stocks of variola virus. It was noted that the variola gene pool could be cloned into non-expressing sites in bacterial plasmids, for future studies of variola virus. Archival records of variola virus would be satisfied by such cloned DNA. The Committee was informed that plasmids encoding variola DNA had been prepared at the Public Health Laboratory Service Centre for Applied Microbiology and Research, Porton Down, Salisbury, United Kingdom and at the Centers for Disease Control, Atlanta, United States. The plasmids are classed at Biosafety level 1. DNA had been cloned from 2 strains of variola major (Harvey and Bangladesh), 2 strains of alastrim (Garcia and Butler) and 1 strain of African variola minor (Somalia), but in no case had the cross-linked terminal fragments been cloned and the full series of internal fragments from Butler was still in the course of construction. The Committee considered that it was not

Because implementation of a decision to destroy all variola virus stocks could be irrevocable, some 60 virologists working in 21 countries had been consulted by a Committee member before the meeting; only 5 thought that variola virus should be maintained indefinitely.

Taking these facts into consideration, the Committee concluded that the cloned DNA provided sufficient reference material to resolve any future diagnostic problem involving suspected smallpox and that research studies of variola requiring culture of the virus were no longer justified. Thus, in the Committee's opinion, there was no need to retain stocks of viable variola virus any longer.

5. Monkeypox surveillance and research (Global Commission recommendation 11)

The number of human monkeypox cases detected each year since 1980 was reported as follows: 1981, 8; 1982, 39; 1983, 84; 1984, 89; 1985, 55 (provisional figure). Six of the cases detected in 1984 occurred in the Central African Republic, but the rest occurred in Zaïre. Thus studies of the epidemiology and ecology of monkeypox virus have concentrated on 5 areas in Zaïre where cases had been detected in previous years.

Routine smallpox vaccination was effectively discontinued in Zaïre in 1980, so that a susceptible cohort of children now aged 0-5 years is present throughout these areas.

The number of cases detected in 1983 and 1984 was higher than in previous years but this is believed to be due to improved surveillance. In 1985 the number of cases declined despite an increasing number of susceptible children; the age distribution of cases did not change and secondary attack rates diminished.

A stochastic model has been developed based on the records of secondary cases occurring in contacts who were or were not vaccinated and who did or did not live in the same household as the index case. The model was validated by the closeness of its predictions to the observed numbers. It was used to extrapolate the probability of continuing spread of monkeypox virus as vaccination immunity declined to 50% and to 0%. Even in the absence of vaccination the model predicted that outbreaks would be self-limiting and not significantly larger than those recently experienced.

Ecological studies of the reservoir of monkeypox virus have advanced rapidly in the last 2 years and include the first isolation of this virus from an animal caught in the wild.¹ The animal concerned was a small squirrel (*Funisciurus anerythrus*), a species which is abundant among the oil palms found in agricultural land separating villages from the primary forest.

Epidemiological investigations suggest that many human monkeypox infections were acquired in this environment and the existence of transmission of the virus among squirrels has been confirmed by the demonstration that between 14% and 20% of over 300 squirrels captured in this area had monkeypox-specific antibody.²

Intensive surveillance activities have covered a population of about 5 million people. With the very low incidence rate of human monkeypox, and growing confidence that this virus cannot sustain itself by human-to-human spread, the Committee believes that it does not pose a significant health problem. This view is strengthened by the recognition that sporadic cases of human monkeypox must have occurred over a long period without a variant arising which was capable of sustained transmission in humans.

The Committee congratulated the authors of the various reports on the monkeypox situation. The Committee recognized that human monkeypox and its ecology pose many interesting and unanswered questions which it hopes may continue to be addressed by the investigators, but believes that, after 1986, this should be considered in the broader context of research priorities in West and Central Africa.

6. Laboratory investigations (Global

the expertise to assist with the diagnosis of suspect cases and supporting studies on the ecology of monkeypox virus. The Committee foresaw that cooperation would develop between the WHO collaborating centres and other laboratories which were interested in monkeypox or in developing new techniques applicable to serological diagnosis or in other ways. The Committee noted that a Japanese team had recently visited Zaïre and entered into an agreement to support surveillance activities on a bilateral basis.

The Committee commended WHO for its coordination of laboratory diagnosis and research on orthopoxviruses during the period following the confirmation of smallpox eradication. This has permitted the accumulation of valuable information and contributed to the present assurance that smallpox eradication is complete.

7. Documentation of the Smallpox Eradication Programme (Global Commission recommendations 16 and 17)

The Committee was informed about the progress made towards publication of the book "Smallpox and its Eradication" which it is hoped will be in print in time for the tenth anniversary of the last endemic case of smallpox, in October 1987.

Most of the files relating to smallpox had been catalogued by a professional archivist, but the Committee noted that more archival work would be necessary when preparation of the book was completed.

8. Central coordination at WHO headquarters (Global Commission recommendations 18 and 19)

The Committee was told that a Smallpox Eradication unit had been maintained at WHO headquarters with a staff complement approximating that outlined by the Global Commission. WHO planned to discontinue this unit at the end of 1987.

As noted earlier, a Committee on Orthopoxvirus Infections had been established in 1981 and had met in 1982, 1983, 1984 and 1986. It was considered that there was no further need for such a committee, but that WHO might need to set up ad hoc committees at various times to consider specific problems that might arise.

Conclusions and recommendations

The Committee, having considered in detail the implementation of the 19 recommendations of the Global Commission, concluded that the success of smallpox eradication was assured and that the actions recommended by the Global Commission were almost completed.

In October 1987, 10 years will have elapsed since the occurrence of the last case of endemic smallpox—a more than adequate period of time to provide full assurance that naturally occurring smallpox will not recur. Between April 1986 and October 1987, several actions are foreseen: (1) the book "Smallpox and its Eradication" should be published; (2) DNA fragments of further selected strains of variola virus should be cloned; (3) WHO-supported field studies of the ecology of monkeypox virus should continue to the end of 1986, with full expectation that responsibilities for field studies would then be assumed by others; and (4) necessary arrangements should be made to place the records of the programme in a permanent archive.

jouer en mettant leurs compétences au service du diagnostic des cas suspects et en appuyant des études portant sur l'écologie de l'orthopoxvirus simien. Le Comité prévoit qu'une coopération se développera entre les centres collaborateurs OMS et les autres laboratoires intéressés par l'orthopoxvirose simienne et par la mise au point de nouvelles techniques applicables notamment au diagnostic sérologique. Le Comité a noté qu'une équipe japonaise s'est dernièrement rendue au Zaïre et y a conclu un accord bilatéral qui prévoit un appui aux activités de surveillance.

Le Comité a félicité l'OMS de la façon dont elle a su coordonner les activités de recherche et de diagnostic en laboratoire sur les orthopoxvirus pendant la période qui a suivi la confirmation de l'éradication de la variole. Cela a permis d'accumuler des informations précieuses et contribué à établir avec certitude que l'éradication de la variole est complète.